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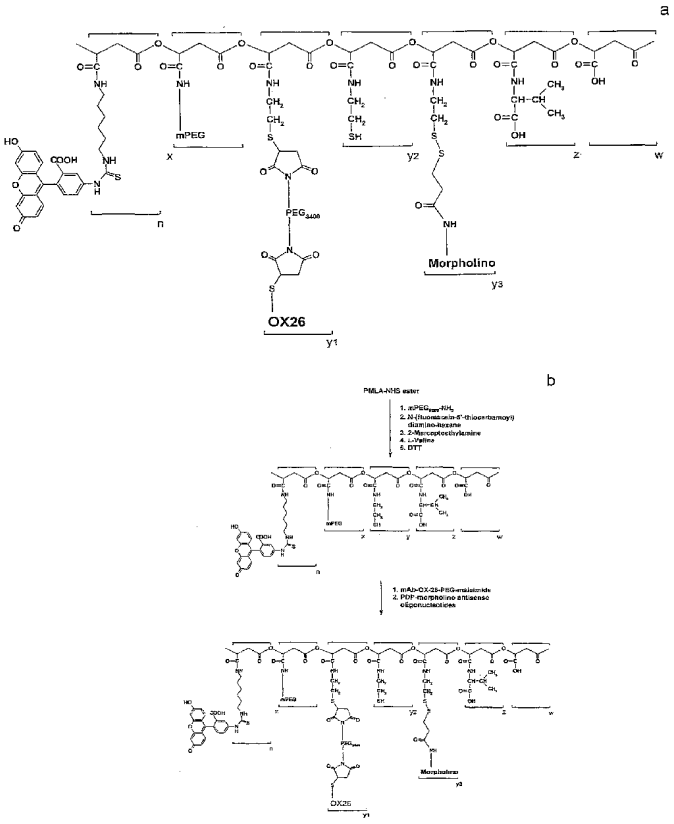
(54) Title: POLYMALIC ACID-BASED MULTIFUNCTIONAL DRUG DELIVERY SYSTEM



(57) Abstract: A structured drug system that is useful for delivering a drug payload to a specific tissue or cell type is disclosed. The system is based on purified polymalic acid. This polymer isolated from natural sources is biocompatible, biodegradable and of very low toxicity. The polymer is extremely water soluble and contains a large number of free carboxyl groups which can used to attach a number of different active molecules. In the examples disclosed N-hydroxysuccinimide esters of the carboxyl groups are used to attach such molecules. The active molecules include monoclonal antibodies to promote specific cellular uptake and specific pro-drugs such as antisense nucleic acids designed to modify the cellular metabolism of a target cell. The pro-drugs are advantageously linked by a somewhat labile bond so that they will be released under specific conditions. In addition, the system contains amide-linked valine to encourage membrane disruption under lysosomal conditions. Polyethylene glycol groups are attached to extend the drug system's circulation half-life. In addition, fluorescent reported groups can be readily included to aid in visualizing and confirming drug system targeting. The drug system can deliver treatments for a wide range of diseases and is specially advantageous for treatment of neoplasms.

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